

### **REMARKS/ARGUMENTS**

Reconsideration and allowance of the pending claims is respectfully requested in light of the remarks which follow. Claim 1 has been amended to incorporate the limitations of dependent claim 7. Thus, no new matter has been added. Upon entry of this amendment, claims 1, 9, 11-14, 18-22, and 25-30 will be pending.

#### **Claim rejections under 35 U.S.C. § 103(a)**

Claims 1, 4, 8-9, 11-14, 18-22, and 25-30 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Leppla *et al.* (U.S. Patent No. 5,677,274) ("Leppla") as evidenced by Klimpel *et al.* (PNAS, 89:10277-10281 (1992)) ("Klimpel") in view of Bayley *et al.* (U.S. Patent No. 5,817,771) ("Bayley"), Dano (U.S. Patent No. 5,519,120) ("Dano"), and Coombs *et al.* (J. Biol. Chem., 273:4323-4328 (1998)) ("Coombs"). To the extent that this rejection applies to the amended claims, Applicants respectfully traverse.

As set forth in greater detail in the previous Office Action response, the *Graham* factors, including the use of objective evidence of secondary considerations to rebut a *prima facie* case of obviousness, as well as, a flexible use of the teaching, suggestion, motivation test, remains the framework to be followed for a determination of obviousness in light of *KSR*. See *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007).

Furthermore, as set forth in M.P.E.P. § 2143, "[t]o establish a *prima facie* case of obviousness, *three* basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations." All three elements set forth above must be present in order to establish a *prima facie* case of obviousness.

#### **1. The present rejection**

The Examiner has maintained this rejection from the previous Office Action, citing two additional references, Dano and Coombs, to arrive at the present obviousness rejection. In the previous Office Action response, Applicants had amended the claims to recite

administration of the compositions of the invention to "carcinoma or fibrosarcoma" cells in response to the cited combination of Leppa, Klimpel, and Bayley. In the present Office Action, the Examiner acknowledges that the previously cited references did not teach or suggest carcinoma or fibrosarcoma. *See* Office Action at page 6. However, the Examiner now cites Dano as remedying this deficiency by "teach[ing] that u-PA has been found in extracts from human lung, colon . . . and metastasizing Lewis lung carcinomas and fibrosarcoma cells." *See* Office Action at page 4. Furthermore, with respect to claim 7, the Examiner identifies Coombs as the closest prior art, as it "teaches a uPA cleavage site consisting of the amino acid sequence PGSGRSAG". *See* Office Action on page 8. However, as stated by the Examiner, "the prior art does not appear to provide any motivation to remove the glycine from the prior art sequence to arrive at the claimed invention. As such, claim 7 appears to be free of the prior art, but is objected to as being dependent from a rejected independent claim." *See* Office Action on pages 8-9, bridging paragraph.

2. The combined references do not teach each and every element of the claimed invention

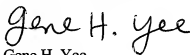
In the interest of expediting prosecution, Applicants have amended claim 1 to recite, in part, "wherein the uPA-recognized cleavage site is PGSGRSA (SEQ ID NO: 5)". Applicants agree with the Examiner that none of the cited references, singly or in combination, teach or suggest this element of claim 1 as amended. Thus, at a minimum, the cited references do not teach or suggest all the claim limitations of amended claim 1, as required to establish a *prima facie* case of obviousness. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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